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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,467	03/30/2004	Anna Marie Aguinaldo	5103-US-01	7268

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XENCOR
111 W. LEMON AVENUE
MONROVIA, CA 91016

EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
09/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,467	AGUINALDO ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *6/10/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/30/2004 and 11/082004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence compairson*.

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 1/10/2008, including arguments/remarks and amended claims, was received on 6/10/2008 and has been entered into the record.

2. In the response received on 6/10/2008, the Applicants cancelled claims 1-15 and added new claims 16-26. Claims 16-26 are therefore pending and are the subject of this office action.

Claim Objections

1. Objection to original claims 1-5, as set forth on page 3 of the office action mailed on 1/10/2008, is moot in view of Applicants' cancellation of the claims.

2. Claim 16 is objected to because it is not clear if the non-polypeptide moiety is not conjugated to position 8 of the variant interferon (IFN) polypeptide, or the wild-type IFN polypeptide. It is also not clear how a non-polypeptide moiety could be conjugated, or not conjugated, to a description of a mutation rather than the position itself (i.e. there is no "F8E" within an IFN-β polypeptide, but rather a phenylalanine or a glutamic acid at position 8).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Rejection of claims 1-5 under 35 USC § 101 as being directed towards non-statutory subject matter, as set forth on page 3 of the prior office action mailed on 1/10/2008, is withdrawn in response to Applicants' cancellation of these claims and submission of new claims 16-26 which are drawn to an *isolated* variant type I IFN.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 16-26 *are rejected* under 35 USC § 112, first paragraph, regarding lack of enablement for variant IFN-β polypeptides comprising unlimited modifications, as originally applied to claims 1-5, as set forth on pages 3-5 of the office action mailed on 1/10/2008.

In the response received on 6/10/2008, the Applicants argue that new claims 16-26 are drawn to variant IFN-β polypeptides comprising substitution at position 8, which was indicated as enabled in the office action of 1/10/2008, and therefore the currently pending claims are enabled by the specification.

These arguments have been fully considered and are not persuasive. As written, independent claim 16 recites an isolated IFN-β variant *comprising* a F8E substitution, and therefore is not limited to the F8E substitution. Although the specification provides guidance and examples of IFN-β polypeptides with F8E, F111N, L5Q, L116E, and/or L120R substitutions, there is no guidance or examples of IFN-β polypeptides comprising substitution at any other position, wherein said IFN-β polypeptides exhibit greater solubility compared to the wild-type IFN-β polypeptide. The specification does not teach which amino acid residues, other than F8, L5, F111, L116, and L120, can be altered and still produce a polypeptide with the desired features. As set forth in the previous office action, one of ordinary skill in the art would know that mutation of a given protein can be associated with unpredictable effects on biological activity, and therefore a skilled artisan would not be able to predict which substitutions, other than the F8E, L5Q, F111N, L116E, and/or L120R substitutions, would produce an IFN-β polypeptide with greater solubility compared to the wild-type polypeptide. For these reasons, one of ordinary skill in the art would require further, undue experimentation in order to make and use all possible variant IFN-β polypeptides *comprising* an F8E substitution and exhibiting greater solubility compared to the wild-type IFN-β polypeptide.

2. Rejection of claims 1-5 under 35 USC § 112, first paragraph, regarding lack of enablement for variant IFN-β polypeptides comprising the recited substitutions and exhibiting increased immunogenicity, as set forth on page 5 of the office action mailed on 1/10/2008, is *withdrawn* in response to Applicants' cancellation of claims 1-5, and submission of new claims 16-26 which do not recite this limitation.

Claim Rejections - 35 USC § 112, first paragraph – written description

1. Claims 16-26 *are rejected* under 35 USC § 112, first paragraph, regarding lack of written description for variant IFN-β polypeptides comprising unlimited modifications, as originally applied to claims 1-5, as set forth on page 6 of the office action mailed on 1/10/2008.

In the response received on 6/10/2008, the Applicants argue that new claims 16-26 recite variant IFN-b polypeptides which have been described in the specification.

This argument has been fully considered and is not persuasive. New claims 16-26 are drawn to isolated IFN-β variants *comprising* an F8E substitution, wherein said variants exhibit greater solubility compared to the wild-type IFN-β polypeptide. Due to the open-ended language of independent claim 16, which recites a variant comprising an F8E substitution, the claimed variants are not limited to IFN-β polypeptides with a F8E substitution, or any of the other recited substitutions. The specification describes variant IFN-β polypeptides with substitutions at position F8, L5, F111, L116, and/or L120. However, there is no description of IFN-β polypeptides comprising substitution at any other position, wherein the resulting IFN-β exhibits increased solubility compared to the wild-type IFN-β polypeptide. Furthermore, there is no description of any other amino acid residue or region within the IFN-β polypeptide of SEQ ID NO: 15 that can be altered, or any description of which amino acid residues must be conserved in order to exhibit greater solubility than the wild-type polypeptide. Accordingly, the instant specification does not adequately describe all possible IFN-β polypeptides *comprising* the F8E substitution and exhibiting greater solubility compared to the wild-type IFN-β polypeptide of SEQ ID NO: 15.

2. Claims 16-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

Independent claim 16 recites an isolated variant IFN-β polypeptide comprising an F8E substitution and exhibiting increased solubility compared to a wild-type IFN-β polypeptide, and "wherein a non-polypeptide moiety is not conjugated at F8E". After extensive review, the Examiner is unable to find, in the Specification as originally filed, support for this newly added limitation of a non-polypeptide moiety not conjugated at F8E. This newly added limitation is not expressly asserted, nor does it flow naturally from the Specification as originally filed.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of claims 1-5 under 35 USC § 112, second paragraph, as being indefinite regarding the metes and bounds of "position 8" of an IFN-β polypeptide, as set forth on page 7 of the office action mailed on 1/10/2008, is *withdrawn* in response to Applicant's cancellation of the claims, and submission of new claims 16-26 which recite variants arising from an F8E substitution of the polypeptide identified by SEQ ID NO: 15.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejections withdrawn

1. Rejection of claims 1-4 under 35 USC § 102(b) as being anticipated by Runkel *et al* (*Biochem.* 2000, Vol. 39, p. 2538-2551), as set forth on pages 7-8 of the office action mailed on 1/10/2008, is *withdrawn* in response to Applicants' cancellation of claims 1-4, and submission of new claims 16-26 which are drawn to isolated IFN-β variants comprising an F8E substitution. Because Runkel does not disclose any IFN-β polypeptide comprising an F8E substitution, new claims 16-26 are not anticipated by Runkel *et al*.

2. Rejection of claims 1-4 under 35 USC § 102(e) as being anticipated by Pedersen *et al* (US 6,531,122), as set forth on pages 8-9 of the office action mailed on 1/10/2008, is *withdrawn* in response to Applicants' cancellation of claims 1-4 and arguments that Pedersen teaches that mutation at position F8 is

one of many possibilities, and that Pedersen teaches polypeptides that comprise a non-polypeptide moiety conjugated to the substituted amino acid.

These arguments have been fully considered. It is noted that while Pedersen teaches substitution at position F8 as one of several possible substitutions, it nonetheless discloses this substitution. However, Pedersen does not specifically disclose an F8E substitution of IFN-β without conjugation to a non-polypeptide moiety. Therefore, Pedersen does not meet the limitations of currently pending claims 16-26 as currently written.

3. Rejection of claims 1-4 under 35 USC § 102(b) as being anticipated by Bell *et al* (US 4,738,844), as set forth on pages 9-10 of the office action mailed on 1/10/2008, is *withdrawn* in response to Applicants' cancellation of claims 1-4, and submission of new claims 16-26, which are drawn to isolated IFN-β variants comprising an F8E substitution. Bell does not disclose an IFN-β polypeptide comprising an F8E substitution, and thus does not anticipate new claims 16-26.

Rejection necessitated by amendment

4. Claim 16 is rejected under 35 U.S.C. 102(e) as being anticipated by Gantier *et al* (US 20040132977). New claim 16 is drawn to an isolated IFN-b variant based on the sequence of SEQ ID NO: 15, wherein said variant comprises an F8E substitution.

Gantier *et al* teaches a polypeptide, SEQ ID NO: 1122 that is 99.2% identical to SEQ ID NO: 15 of the instant application, and comprises a glutamic acid substituted for the phenylalanine normally found at position 8 (see sequence comparison). Therefore, Gantier *et al* teaches an IFN-β polypeptide based on the sequence of SEQ ID NO: 15 and comprising an F8E substitution. Although Gantier *et al* does not explicitly teach that this polypeptide exhibits increased solubility compared to the wild-type IFN-β polypeptide, it would be expected, in the absence of evidence to the contrary, that this polypeptide would exhibit increased solubility because the instant specification teaches that this is a feature of IFN-β polypeptides comprising an F8E substitution. Because the USPTO does not have the facilities for testing the solubility of the polypeptide of Gantier *et al*, the burden is on the Applicants to show a novel and unobvious difference between the claimed IFN-β variant and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, because Gantier *et al* teaches an IFN-β polypeptide comprising an F8E substitution, wherein this polypeptide would be expected to inhibit increased solubility compared to the wild-type IFN-β polypeptide, Gantier *et al* meets the limitations of claim 16.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Rejection of claims 1-5 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 7, 10-12, 27-28, and 35 of Application No. 10/676,705, as set forth on page 10 of the office action mailed on 1/10/2008, is *withdrawn* in view of Applicants' cancellation of claims 1-5 and the abandonment of the '705 application.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647